

## **REMARKS/ARGUMENTS**

### **I. Status of Claims**

Claim 113 is amended to recite HER-2/neu, to replace the previous recitation of Her2 or Her-2. Claim 123 is amended to recite 3D-MPL, replacing the recitation of "3d-MPL." Claim 113, 127, and 138 are also amended to recite a 90% amino acid sequence identity to a reference sequence. This percentage identity finds support in the specification, *e.g.*, on page 9, lines 27-32. Furthermore, claims 113, 127, and 138 are amended to recite a fusion protein "consisting of" a HER-2/neu extracellular domain linked to a HER-2/neu phosphorylation domain to clarify that the only HER-2/neu components of fusion protein are those two domains. Pending claims are further amended to ensure proper antecedent basis. No new matter is introduced by the present amendment.

### **II. Claim Rejections**

#### **A. 35 U.S.C. § 112, Second Paragraph**

Claims 113-144 were rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness for failing to point out and distinctly claim the subject matter. Applicants respectfully traverse the rejection in light of the present amendment.

The first reason for the rejection, according to the Examiner, is that Claim 113 recites "HER-2," "Her2," and "Her-2" and the specification uses "HER-2." As recommended by the Examiner, Claim 113 has been amended to change "Her2" and "Her-2" to "HER-2." The second reason for the rejection, according to the Examiner, is that Claim 123 recites "3dMPL" and the specification uses "3D-MPL." As recommended by the Examiner, Claim 123 has been amended to recite "3D-MPL," instead of "3dMPL." As such, Applicants submit the definiteness requirement has been met and respectfully request the withdrawal of the rejections for Claim 113 and all dependent claims and Claim 123 and dependent Claim 124 under 35 U.S.C. §112, second paragraph.

B. 35 U.S.C. §112, First Paragraph: Written Description

Claims 113 and all dependent claims (113-125) were rejected under 35 U.S.C. §112, first paragraph, for alleged failure to meet the written description requirement. Applicants respectfully traverse the rejection in light of the present amendment.

The reason of the rejection, according to the Examiner, is that the claimed fusion proteins as defined by the hybridization conditions are not described in the specification and is therefore new matter. Although Applicants disagree with the Examiner and have previously described the page and line number in the specification that supports these conditions, to expedite prosecution, pending claims have been amended to delete the recitation of hybridization under specified conditions with reference polynucleotide sequences. As amended, pending claims now recite a HER-2/neu fusion protein that consists of an extracellular domain (ECD) and a phosphorylation domain (PD) and has an at least 90% amino acid sequence identity to SEQ ID NO: 6. The written description rejection on the ground of new matter is thus obviated.

Claims 113-144 were also rejected, by the Examiner, under the written description requirement for allegedly failing to adequately describe the claimed genus (Office Action, p 6. The pending claims as amended fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, “[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . .” *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description “requires a precise definition, such as by structure, formula, chemical name, or physical properties.” *Fiers*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Finally, the MPEP states that structural formulas provide a convenient method of demonstrating possession of specific molecules. MPEP §2163.

It is a structural property of a nucleic acid to encode a polypeptide comprising a fusion protein that has a high degree of sequence identity to a reference amino acid sequence, because the amino acid sequence of the polypeptide is directly determined by the polynucleotide

sequence of the nucleic acid. Claims 113, 127 and 138 (and hence their dependent claims) set forth well-defined structural features of the claimed genus of nucleic acids, *i.e.*, encoding a polypeptide comprising a HER-2/neu fusion protein that consists of an ECD and a PD and has at least 90% identity to the amino acid sequence of SEQ ID NO:6.

Applicants submit, therefore, that the claimed nucleic acids are thereby defined via shared structural properties and described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Such description is consistent with the standards set forth in *Lilly*. As such, Applicants submit the written description requirement is met and respectfully request the withdrawal of the rejections under 35 USC §112, first paragraph.

C. 35 U.S.C. §102

***1. Disis et al.***

Claims 113, 114, 118, and 121 were rejected under 35 U.S.C. §102(b) for alleged anticipation by Disis *et al.* (IDS, 1996, 156 J. IMMUNOLOGY 3151-8). Applicants respectfully traverse the rejection in light of the present amendment.

To anticipate a pending claim, a prior art reference must provide all limitations of the claim. MPEP §2131. As amended, independent claim 113 is drawn to method for eliciting or enhancing an immune response to a HER-2/neu fusion protein by administering to a warm-blooded animal a composition which consists of a HER-2/neu extracellular domain (ECD) linked to a HER-2/neu phosphorylation domain (PD), has at least 90% identity to SEQ ID NO:6, and is capable of producing an immune response in a warm-blooded animal. In other words, Applicants disclose a method, which uses a fusion protein consisting of two different linked protein domains from HER-2/neu—one extracellular (ECD) and the other intracellular (the phosphorylation domain). Disis *et al.*, in contrast discloses the use of a mixture of peptides to inoculate rats from either the extracellular region or the intracellular region. The limitation of a HER-2/neu fusion protein consisting of an ECD linked to a PD is not present in the Disis *et al.*

reference, nor is the use of a combination of a mixture of extracellular *and* intracellular protein domains. Therefore, claims 113, as well as its dependent claims, are not anticipated by Disis *et al.* Accordingly, the anticipation rejection should be properly withdrawn.

D. 35 U.S.C. §103

***1. Disis et al. in View of Specification.***

Claims 117, 119, 120, 122-125 were rejected under 35 U.S.C. §103(a) for alleged obviousness over Disis *et al.* as applied to 113, 114, 118, and 121 and in view of Applicants' alleged admission at page 51, line 19-31. Applicants respectfully traverse the rejection in light of the present amendment.

To establish a *prima facie* case of obviousness, three basic criteria must be met: first, the prior art references must teach or suggest all the claim limitations; second, there must be some suggestion or motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to combine the limitations; third, there must be a reasonable expectation of success in combining the limitations. MPEP §2143. Furthermore, the use of Applicant's specification to form an obviousness rejection is impermissible hindsight.

As discussed above, the Disis *et al.* reference does not provide all limitations of independent claims 113, 114, 118, and 121. As such, the combination of Disis *et al.* and the specification together fail to provide all limitations of the pending claims. No *prima facie* case of obviousness has been established. In fact, Disis *et al.* discloses that its data suggest that "cellular immunity could not be elicited by immunization with a vaccinia construct expressing ECD" (at page 3155, paragraph 3 of discussion). This reference teaches away from the current invention. Therefore, the claimed invention would not be obvious to one of skill in the art. Applicants thus respectfully request that the Examiner withdraw the obviousness rejection.

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Amdt. dated June 18, 2004  
Reply to Office Action of December, 18, 2003

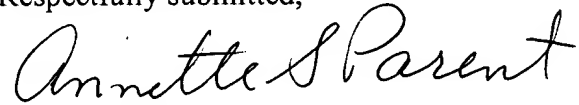
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**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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